B INTERMITTENT CLAUDICATION

B 1 Introduction and Characterization of Patients

B 1.1 Definition and Nomenclature for Intermittent Claudication

The word *claudication* is derived from "claudicatio," meaning "to limp." It is said to have originated when physiologists, studying arterial pressure by cannulating the femoral arteries of horses and then ligating their femoral arteries, observed them to limp before stopping *intermittently*, as they ran in the fields afterwards. The term *intermittent claudication* has thus come to mean leg pain sufficient to cause the patient to stop, which is produced by exercise and relieved by rest, and is caused by arterial occlusive disease. It could be added that the pain is *reproducibly* caused by a given degree of exercise and relieved within minutes by rest. These and other characteristics are discussed further under B 2.1, Clinical Evaluation (p S56) One who claudicates is called a *claudicant*, although the term *claudicator* is also frequently used. Other diseases that cause discomfort with ambulation have been referred to as claudication, as in neurospinal claudication, which is discussed later, but these conditions should either be grouped under pseudoclaudication or be preceded by a defining word such as *neurospinal*. When *intermittent* precedes the word *claudication*, the cause is presumed to be arterial occlusive in origin, although the simpler term *claudication* is mostly used throughout this text.

B 1.1.1 Patient Characteristics

Intermittent claudication (IC) can be caused by any occlusive lesion in the arterial supply of the leg muscles that interferes sufficiently enough with blood flow to produce ischemic pain with exercise. In the Western world at least, it is overwhelmingly the result of atherosclerosis and the focus of this document, PAD. Other causes are discussed later under differential diagnosis (see B 2.1.2, p S57). Those with IC from PAD will be predominantly older patients, predominantly male, and almost invariably with identifiable risk factors for atherosclerosis, as previously detailed in A 2.2, Epidemiology—Intermittent Claudication (p S5).

Also detailed earlier (Epidemiology, A 2.4 and A 2.5, pp S15 and p S18) are the facts that, in contrast to patients with chronic critical limb ischemia, those with IC tend to have single rather than multi-level disease, to be somewhat younger, to have less atherosclerotic disease elsewhere, and a better longevity outlook (in terms of remaining years, not age at death). They also have a much more benign outlook for future limb loss. These characteristics should be kept in mind in reading the subsequent sections. It also should be remembered that IC depends on activity level. Those with arthritis and other conditions preventing ambulation and otherwise sedentary patients with arterial occlusive disease equivalent to that producing IC in active patients may be completely asymptomatic in this regard.

B 1.1.2 Hemodynamic Abnormalities

The pathophysiology of PAD, whether it produces claudication, rest pain, or tissue loss, is primarily accounted for by the hemodynamic severity and number of occlusive lesions in the peripheral circulation. Hemodynamic significance of an arterial stenosis is a function not only of the percentage stenosis, but also of flow velocity across the lesion.[1,2] For example, at rest, blood flow velocity in the femoral artery may be as low as 20 cm/s. At this velocity, a stenosis will not become hemodynamically significant until it is 90% occlusive. Above 90% stenosis, flow and pressure rapidly decrease with increasing obstruction. However, with exercise in the normal extremity, flow velocity may increase to as high as 150 cm/s. At these higher flow velocities, a stenosis becomes hemodynamically significant at approximately 50%. Thus, patients with claudication have normal flow to skeletal muscle at rest, but markedly impaired flow to meet metabolic demand with exercise.

On average, patients with single-segment disease, such as occlusion of the iliac vessels, and good

collateral development will have mild claudication. With more extensive disease, claudication symptoms become more severe. Symptoms cannot be entirely explained by the severity of reduction in blood pressure. For example, the ABPI in patients with claudication is not well correlated with their exercise performance on a treadmill, or with the severity of symptoms in the community setting.[3,4,5]

B 1.1.3 Metabolic and Neurological Abnormalities

Peripheral arterial disease is not simply a hemodynamic disorder. Additional factors are involved in the pathogenesis of this disease. Key factors include deconditioning, because these patients are very inactive. In addition, several studies have shown skeletal muscle injury in patients with chronic arterial occlusive disease. This injury has been characterized as a distal axonal denervation leading to loss of muscle fibers and mild atrophy of the affected muscle.[6,7] Muscle strength is reduced in these patients, which leads to a compromise of muscle function and exercise performance. In addition, oxidative metabolism is severely impaired in PAD patients, and these changes cannot be accounted for simply by the reduction in blood flow.

Several studies have observed that patients with peripheral arterial disease accumulate intermediates of oxidation such as acylcarnitines.[8] These compounds are formed from acyl-CoA intermediates in the oxidation of fatty acids, proteins, and carbohydrates. This accumulation has functional significance in that patients with the greatest degree of metabolic disruption and accumulation of acylcarnitines have the most severely impaired exercise performance. Further evidence for altered metabolism comes from magnetic resonance spectroscopy. Several studies have indicated that patients with PAD have not only impaired resynthesis of phosphocreatinine, but abnormally high levels of adenosine diphosphate (ADP).[9,10] These findings are consistent with a metabolic myopathy, which occurs in chronic forms of the disease.

In summary, the pathogenesis of PAD is initiated by atherosclerotic occlusions of the major conduit vessels in the lower extremity. However, over time the disease affects the skeletal muscle neurological and metabolic function, leading to further impairments in muscle performance and patient functional status.

References

1. Demer L, Gould KL, Kirkeeide R. Assessing stenosis severity: coronary flow reserve, collateral function, quantitative coronary arteriography, positron imaging, and digital subtraction angiography: a review and analysis. Prog Cardiovasc Dis 1988;30:307-322.
2. Young DF, Cholvin NR, Kirkeeide RL, Roth AC. Hemodynamics of arterial stenoses at elevated flow rates. Circ Res 1977;41:99-107.
3. Arfvidsson B, Wennmalm A, Gelin J, Dahllof AG, Hallgren B, Lundholm K. Co-variation between walking ability and circulatory alterations in patients with intermittent claudication. Eur J Vasc Surg 1992;6:642-646.
4. Hiatt WR, Nawaz D, Regensteiner JG, Hossack KF. The evaluation of exercise performance in patients with peripheral vascular disease. J.Cardiopulmonary Rehabil. 1988;12:525-532.
5. Lorentsen E. Blood pressure and flow in the calf in relation to claudication distance. Scand J Clin Lab Invest 1973;31:141-146.
6. England JD, Regensteiner JG, Ringel SP, Carry MR, Hiatt WR. Muscle denervation in peripheral arterial disease. Neurology 1992;42:994-999.
7. Regensteiner JG, Wolfel EE, Brass EP, Carry MR, Ringel SP, Hargarten ME, et al. Chronic changes in skeletal muscle histology and function in peripheral arterial disease. Circulation 1993;87:413-421.
8. Hiatt WR, Wolfel EE, Regensteiner JG, Brass EP. Skeletal muscle carnitine metabolism in patients with unilateral peripheral arterial disease. J Appl Physiol 1992;73:346-353.
9. Hands LJ, Bore PJ, Galloway G, Morris PJ, Radda GK. Muscle metabolism in patients with peripheral vascular disease investigated by 31P nuclear magnetic resonance spectroscopy. Clin Sci 1986;71:283-290.
10. Kemp GJ, Taylor DJ, Thompson CH, Hands LJ, Rajagopalan B, Styles P, et al. Quantitative analysis by 31P magnetic resonance spectroscopy of abnormal mitochondrial oxidation in skeletal muscle during recovery from exercise. NMR Biomed. 1993;6:302-310.